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A CONTRIBUTION TO THE PROBLEM OF FATTY LIVER FOLLOWING TOTAL PANCREATECTOMY : LABORATORY STUDIES IN DOGS AND MEN

by

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It has been generally believed since FISHER'S report that completely depancreatized dogs usually fail to survive more than six to eight weeks after operation, even if treated adequately with insulin. A marked accumulation of fat in the liver has been found at autopsy to the most prominent change in these dogs.

In case of a malignant tumor growing diffusely in the pancreas, the total pancreatectomy must be performed if it is applicable. But, for the reason of the technical difficulty of the operation, as well as the fear of the possible development of the postoperative fatty liver as observed in the experimental dogs, the total pancreatectomy have been tried in men as few as in about 20 cases in the literature.

In 1934 ENTENMAN, CHAIKOFF and KAPLAN reported that a hypolipemia and a marked lowering of the esterified cholesterol took place in totally depancreatized dogs. They concluded that the cause of the hypolipemia was not the chronic starvation due to the indigestion as a result of the lack of the external pancreatic secretion, but the development of the fatty liver.

In 1924 ALLAN, BOWIE, MACLEOD and ROBINSON reported the beneficial effect of feeding with the raw pancreas tissue in preventing the development of the fatty liver in depancreatized animals, and in 1936 DRAGSTEDT et al expressed the opinion that this effect of the raw pancreas tissue should be accounted for by its content not of pancreatic enzymes or of choline, but of a specific substance, which was believed by them to be a new hormone, named "lipocaic". They stated that the fatty liver was due to lipocaic deficiency and definitely differed from the diabetic fatty liver occurring immediately after pancreatectomy as a result of the inadequate postoperative administration of insulin.

On the other hand, in 1932, BEST and HERSHEY reported that lecithine was effective in preventing the development of the fatty liver and experimental depancreatized dogs treated with lecithine survived many years.

In 1950 MONTGOMERY et al stated that the fatty liver was prevented not only by lipocaic, lecithine or raw pancreas substance but also by crystalline trypsin.

Thus the opinions concerning the pathogenesis of the fatty liver which develops

four to eight weeks after total pancreatectomy are much confused. In order to do total pancreatectomy in men with safety, it is a prerequiste for us to know if 1) the fatty liver may develop in totally pancreatectomized men as in experimental animals, and 2) the fatty liver can be prevented by the administration of certain drugs.

In the present experiments, the development of the fatty liver is predicated during life by the determination of the amount of the serum cholesterol and is confirmed, post mortem, by the quantitative measurement of the total liver lipides together with the histologic fat stain of the liver.

EXPERIMENTALS

Adult dogs, both male and female, were used in this study. Total and subtotal pancreatectomy and pancreatic duct ligation were carried out on these dogs respectively.

METHODS OF OPERATIONS

(1) Total Pancreatectomy : I preferred total pancreatoduodenectomy to simple total pancreatectomy. Therefore in this paper, the term "total pancreatectomy" always means total pancreatoduodenectomy.

(2) Subtotal Pancreatectomy : Nearly total resection of the pancreas (leaving a small portion of the head) was done in one or two stages. The experimental dogs had to be treated with insulin as the postoperative diabetic state usually developed. The remaining portion of the pancreas was found to be about two to three grams at autopsy.

(3) Ligation of the Pancreatic Duct : Double ligations were done at the site of the attachment of the pancreas to the duodenum and then, the pancreatic tissue were divided between these ligatures. Besides, duodenectomy was carried out for the purpose of the complete exclusion of the flow of the pancreatic juice into the gut. After duodenectomy, gastrojejunostomy and choledochojejunostomy were done in the same way as in total pancreatoduodenectomy.

GROUPS OF EXPERIMENTAL DOGS

Experimental dogs were divided into four groups.

Group Ⅰ : This consisted of totally depancreatized dogs of long term survival, which were given an adequate dose of insulin, 5 g of pancreatin and 2 g of methionine per day throughout the postoperative course.

Group Ⅱ : The long survived totally depancreatized dogs, which were treated only with insulin.

Group Ⅲ : The subtotally depancreatized dogs treated with insulin.

Group Ⅳ : The pancreatic duct ligation dogs.

CHAIKOFF et al (1934) reported that in depancreatized dogs the hypolipemia and marked lowering of the esterified cholesterol were observed at the 3rd week after operation and DRAGSTEDT et al (1936) stated that the typical fatty liver was demonstrated in depancreatized dogs, even if treated with insulin adequately, at the 6th 8th week or earlier after operation. Hence, the dogs, which survived longer than 4 weeks after total pancreatectomy, were regarded as being long surviving.

METHOD OF CHEMICAL ANALYSIS AND HISTOLOGICAL STAINING

(1) Colorimetric Analysis of the Serum Cholesterol.

The total serum cholesterol was determined by RAPPAPORT and ENGELBERG'S method and the esterified cholesterol by BLOOR'S method.

(2) Quantitative Determination of the Total Liver Lipides.

Liver lipides were extracted by BLOOR'S method, and the amount of lipides in 100cc. of this extract was determined by the method of VAN DE KAMER A.

(3) Staining of the Fat in the Liver.

Sudan Ⅲ stain was applied to carbowax sections, and in some cases SMITH-DIETHRICH'S lipoid stain was also made.

RESULTS

(I) THE ESTER RATIO OF THE SERUM CHOLESTEROL

(1) Normal Dogs : Normal adult 54 dogs (male : 28, female : 26) were examined and that result were tabulated in Table 1.

Table 1 Ester Ratio of the Serum Cholesterol in Normal Adult Dogs

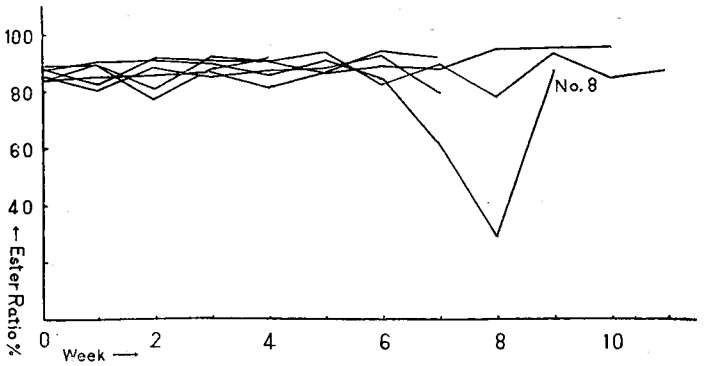
Dog No.	Total chol. mg/dl	Esterified chol. mg/dl	Free chol. mg/dl	Ester Ratio per cent
1	62.6	44.6	18.0	71.2
2	71.4	59.5	11.9	84.7
3	89.6	76.5	13.1	85.3
4	108.6	96.2	12.4	88.5
5	70.4	60.2	10.2	85.5
6	62.4	52.6	9.8	84.2
7	85.7	71.4	14.3	83.3
8	59.6	52.4	7.0	88.2
9	101.0	85.4	15.6	84.5
10	101.0	89.2	11.8	88.4
11	57.8	51.1	6.7	88.4
12	81.3	70.4	10.9	86.6
13	36.4	28.2	8.2	77.4
14	54.8	46.3	8.5	84.1
15	39.2	33.1	6.1	84.2
16	50.5	44.2	6.3	87.5
17	125.8	106.5	19.3	84.6
18	93.0	82.9	10.1	89.1
19	45.2	35.9	9.3	79.3
20	72.4	63.3	9.1	87.4
21	54.4	48.8	5.9	89.1
22	48.0	41.3	6.7	86.0
23	42.2	36.2	6.0	86.2
24	47.2	41.7	5.5	84.1
25	86.2	73.5	12.7	85.2
26	64.4	57.7	6.7	89.6
27	67.2	59.5	7.7	88.5
28	67.5	54.1	13.4	80.1
29	63.2	55.6	7.6	87.9
30	133.0	108.7	24.3	81.7
31	79.6	65.3	14.3	82.0
32	58.4	52.1	6.3	89.2
33	61.7	53.7	8.0	87.0
34	141.8	118.3	23.5	83.7
35	82.6	71.9	10.7	87.0
36	52.1	42.0	10.1	80.6
37	43.8	37.8	6.0	84.0
38	58.8	41.3	17.5	70.2
39	78.1	69.4	8.7	88.9
40	51.5	46.3	5.2	89.9
41	113.6	90.9	22.7	80.1
42	69.8	60.2	9.6	86.3
43	64.6	57.4	7.2	88.9
44	121.2	106.9	14.3	88.2
45	121.9	108.1	13.8	88.9
46	127.3	110.5	16.8	86.8
47	54.4	48.5	5.9	87.1
48	105.2	89.2	16.0	84.8
49	172.8	150.3	22.5	86.9
50	106.3	93.4	12.9	87.9
51	114.2	102.3	11.9	89.5
52	104.7	93.4	11.3	89.2
53	84.0	71.8	12.2	85.5
54	158.9	138.9	20.0	88.8

The quantities of both the total and the esterified cholesterol fluctuated within a relatively wide range, but the ester ratio, which was the quotient of the total

cholesterol to the esterified cholesterol, was almost always 80 per cent to 89 per cent, only in 3 cases the ester ratio was under 80 per cent.

(2) **Group Ⅰ Dogs** : This group consisted of 6 dogs, and the ester ratio of the serum cholesterol varied within the physiologic range (Fig. 1). In No. 8, the ester ratio decreased in the period from the 6th to 7th weeks postoperatively, but it returned to the normal level at the 8th week.

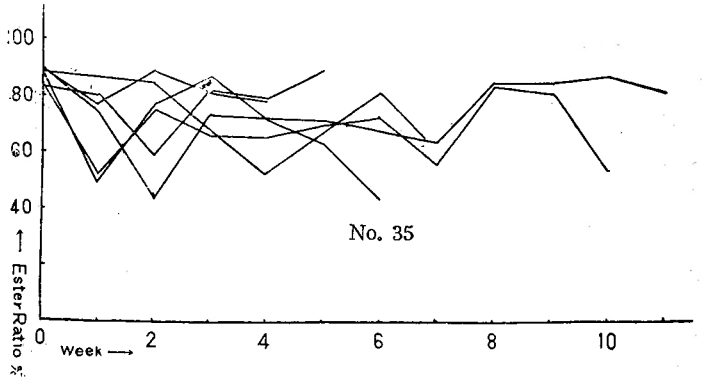
Fig. 1. Ester Ratio in Group Ⅰ



Marked decrease in the ester ratio resulting from the development of the fatty liver has never been observed in this experiment, and there was no case in which the development of the fatty liver was suspected.

(3) **Group Ⅱ Dogs** : This group consisted of 6 dogs. The ester ratio fluctuated within a wider range than in group I, and was almost always under 80 per cent. But the gradual fall to zero in the ester ratio has never been observed also in this group (Fig. 2). Only in No. 35, the development of the fatty liver was suspected, because the ester ratio gradually declined to 45.2 per cent at the 6th week after operation. But the ester ratio in other dogs was maintained within the physiologic range at the time of the determination in the last week, and therefore, the development of the fatty liver was quite improbable in these cases.

Fig. .2 Ester Ratio in Group Ⅱ



(4) **Group Ⅲ Dogs** : This group consisted of 4 dogs. The ester ratio remained within the physiologic range throughout the course of the experiment. Although the dogs were treated only with insulin, the marked lowering of the ester ratio did not occur (Fig. 3). This fact seems to show the distinct difference between the total and the subtotal pancreatectomy.

(5) **Group Ⅳ Dogs** : 4 dogs belonged to this group, and 2 of them received pancreatin and methionine and the other 2 were not treated with these drugs. The ester ratio remained within the physiologic range in the former two and declined

gradually in the course of time in the latter two (Fig. 4). This is the difference, which was also recognized in totally depancreatized animals (Groups I and II).

(6) Totally Depancreatized Men : The determination of the serum cholesterol was made in cases Nos. 2, 3 and 4.

Case No. 2 : A woman aged 39 had been suffering from the dull pain and the feeling of fullness in the epigastrium for about 1 month. For a pancreatic tumor, total pancreatectomy was performed on August 25, 1951. Histologic diagnosis of the tumor was cylindrical-epithelial carcinoma. In this case I was unable to determine the amount of the serum cholesterol preoperatively. After operation, the ester ratio was 87.6 per cent at the 5th week and since then her ester ratio has always been within the physiologic range until now for about 3 years (Fig. 5). She remains healthy now with injection of 28 units of crystalline insulin per day.

Fig. 3. Ester Ratio in Group Ⅲ

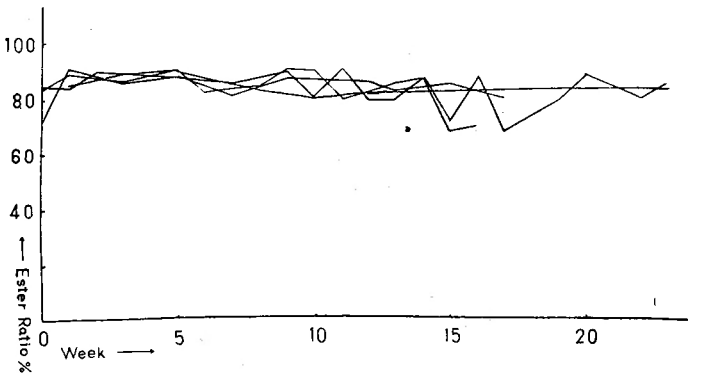


Fig. 4. Ester Ratio in Group Ⅳ

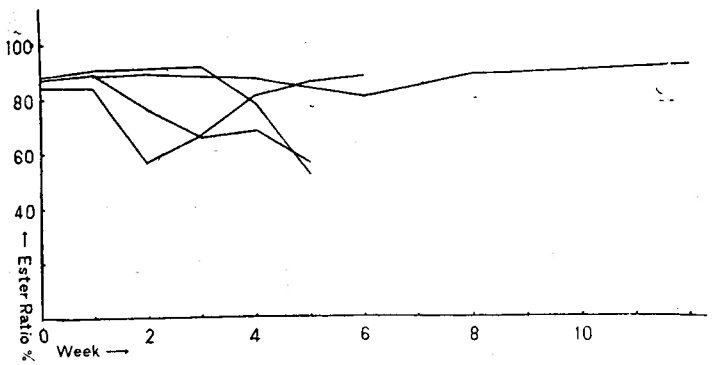
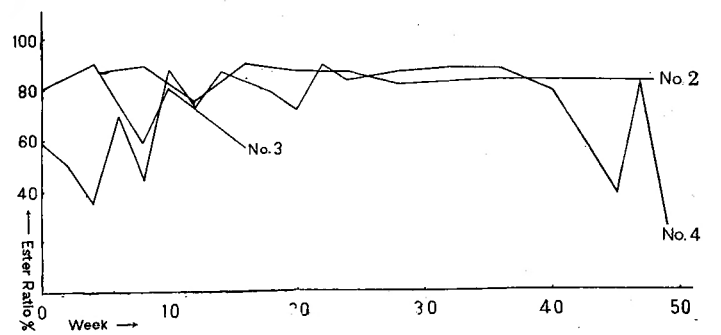


Fig. 5. Ester Ratio in Totally Depancreatized Men.



Case No. 3 : A woman aged 46 had complained of dull epigastrial pain since about 1 month prior to the admission and a painless tumor was palpable in the epigastrium. The preoperative ester ratio was 80 per cent (Fig. 5). Total pancreatoduodenectomy was performed on December 5, 1951. Histologic diagnosis of the pancreatic tumor was pancreatitis interstitialis chronica. Immediate postoperative course was uneventful, but 8 weeks after operation the loss of appetite and a

light sign of stenosis of the intestine appeared gradually. The ester ratio declined to 58.8 per cent at that time, and then, she began to suffer from severe diarrhea at the 11th week after operation. The diarrhea persisted in spitc of various treatments, and the ester ratio declined further to 50 per cent. She died on the 172nd day after operation and the fatty liver was found at autopsy.

Case No. 4 : A man aged 59 had been suffering from obstructive jaundice of about 3 months duration. The preoperative ester ratio was as low as 58.8 per cent (Fig. 5), suggesting a moderately severe hepatic damage. Total pancreato-duodenectomy was performed on September 4, 1952. Moderate degree of liver cirrhosis was found at operation. Histologic diagnosis of the pancreatic tumor was cylindrical-epithelial carcinoma of the head of the pancreas.

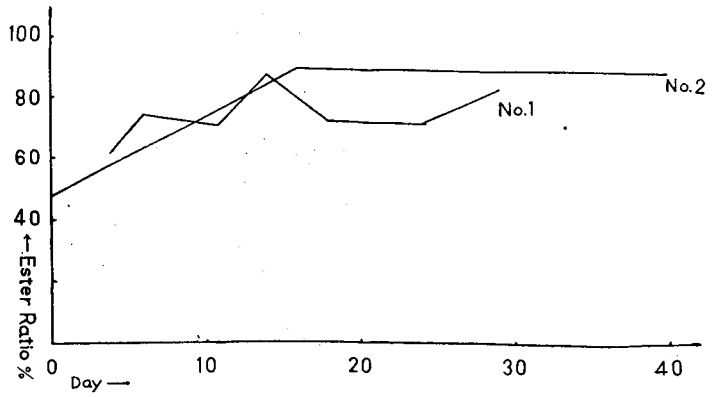
The patient became delirious for several days after the third day following operation, and the ester ratio fluctuated under the normal range. On the 38th postoperative day the patient was suddenly attacked by a hypoglycemic shock with convulsion, which was apparently caused by the injection of 12 units of protamine zinc insulin per day and improved by immediate intravenous administration of hypertonic glucose solution and blood transfusion. Insulin was not given during 3 days after this attack until the patient recovered from hypoglycemia. Then we started again the injection of insulin, gradually increasing the dosis. Another attack of tonic spasms of muscles occurred on the 49th postoperative day, but because the blood sugar was 447mg/dl at that time, the attack did not seem to be the hypoglycemic shock and was settled by intravenous injection of calcium. Afterward the general condition of the patient improved very much and the ester ratio returned to the physiologic level at the 9th week after operation for the first time. But several months later, severe diarrhea appeared accompanied by signs of liver cirrhosis and the patient died on the 344th postoperative day in the condition of uremia.

(7) Human Case of Resection of the Pancreatic Head together with Removal of the Entire Duodenum without Placing Pancreato-Enterostomy :

Case No. 1 : A man aged 64 had suffered from the feeling of fullness and the dull pain in the epigastrium and the nausea after meal for about 3 weeks. For stomach carcinoma involving the pancreas, total gastrectomy and resection of the pancreatic head together with duodenectomy were carried out on July 31, 1951. Pancreato-enterostomy was not done. Histologic diagnosis of the resected specimen was adenocarcinoma of the stomach and its infiltration into the pancreas. Ten days after operation there developed a pancreatic fistula and he died of heavy bleeding from the fistula on the 30th postoperative day.

Case No. 2 : A man aged 32. The obstructive jaundice of 3 months duration. The preoperative ester ratio was 47.0 per cent. Resection of the head of the pancreas combined with total duodenectomy was carried out on October 12, 1952. No anastomosis was made between the remaining pancreas and the intestine. Histologic diagnosis of the resected pancreas was cylindrical-epithelial carcinoma. Postoperative course was uneventful and the ester ratio returned to the normal level at the 2nd

Fig. 6. Ester Ratio in Patients in whom the Resection of the Pancreatic Head was done together with Total Duodenectomy without making Pancreato-Enterostomy.



week after operation (Fig. 6), and he is in good health now.

(II) TOTAL LIVER LIPIDES AND HISTOLOGIC FAT STAIN OF THE LIVER

(1) **Normal Dogs** : 41 adult dogs, male 22, female 19, were examined. The results were tabulated in Table 2.

Findings of the Sudan III stain of the liver : Fine orange red fat granules were present within all parenchymal cells of the liver which were stained violet. Besides, in about a half of the cases, these granules were found in KUPPER'S cells and in some cases also in epithelial cells of the intrahepatic bile ducts.

(2) **Group I Dogs** : Considering from the results of determination of the serum cholesterol, it may be assumed that there is no fatty liver in this group. The assumption was confirmed by the actual determination of the total lipides and the Sudan III stain of the liver tissue obtained at autopsy. The total lipides of the liver were within the physiologic range in all cases (Table 3). The fatty degeneration or infiltration of the liver was not detected by histologic examination (Fig.A). Hence it has become evident that the fatty liver which is expected to occur after total pancreat-

Table 3 Total Liver Lipides in Group I

Dog No.	Total liver lipides: Biopsy at operation g/100g	Total liver lipides: at autopsy g/100g	Survival time days
5	—	2.61	54
8	—	2.36	66
18	3.95	3.76	84
40	2.87	3.19	40
47	5.37	3.54	53

Table 2 Total Liver Lipides in Normal Adult Dogs.

Dog No.	Total Liver Lipides g/100g
7	3.11
11	4.09
12	3.29
13	5.63
14	4.09
15	3.20
16	2.70
17	4.47
18	3.95
19	4.34
21	3.96
22	4.42
23	4.66
24	4.45
26	4.43
27	3.16
28	4.13
29	3.22
30	3.96
33	3.04
34	3.26
35	3.30
36	3.13
37	3.32
38	4.37
39	2.09
40	2.87
41	3.35
42	3.25
43	3.38
44	3.78
45	3.80
47	5.37
48	3.45
49	3.00
51	3.51
53	3.71
55	4.34
56	4.13
58	4.86
59	4.37

ectomy can be prevented completely by the administration of pancreatin and methionine.

(3) **Group Ⅱ Dogs** : The data in 5 dogs were within the normal range. But marked increase in the total liver lipides was found exceptionally in No. 35 (Table 4). In this case the ester ratio declined to 45.2 per cent at the 6th week after operation, suggesting the development of the fatty liver, which was confirmed by autopsy. Intense fatty degeneration of the liver was observed by Sudan III stain only in this case (Fig.C), but not in other 5 dogs, although intracellular fat granules tended to be more abundant in this group than in the Group I (Fig.B).

Table 4 Total Liver Lipides in Group II

Dog No.	Total liver lipides		Survival time days
	Biopsy at operation g/100g	at autopsy g/100g	
26	4.43	3.12	74
28	4.13	3.12	79
35	3.30	12.4	46
37	3.32	4.48	47
41	3.35	5.34	40
43	3.38	4.64	33

(4) **Group Ⅲ and Group Ⅳ Dogs** : Neither increased total liver lipides nor fatty changes of the livers were found in all cases of these two groups, whether pancreatin and methionine might be administered or not (Table 5).

Table 5 Total Liver Lipides in Groups III and IV

Dog No.	Total liver lipides		Survival time days
	Biopsy at operation g/100g	at autopsy g/100g	
7	3.11	3.59	198
9	—	3.29	125
6	—	2.32	36
10	—	2.83	40
16	2.70	2.10	45
60	4.32	5.08	93

(5) **Totally Depancreatized Men** :

Case No. 1 : Only the Sudan III stain of the liver was done. The patient died of the recurrence of carcinoma on the 142nd postoperative day. The liver tissue was generally atrophic and there was the infiltration of carcinoma cells in some parts. The fatty infiltration and degeneration took place in carcinoma cells and in closely neighbouring parenchymal cells of the liver, but not in other parts, and therefore, the development of the fatty liver was excluded (Fig.D).

Case No. 3 : The patient died on the 172nd postoperative day. She had suffered from chronic diarrhea which was not cured by all means. The development of the fatty liver was strongly suspected from the fact that the ester ratio of the serum cholesterol declined to 50 per cent at the 11th postoperative week. The total liver lipides to 17.2g/100g and the remarkable central fatty degeneration of the liver was observed (Fig.E). But since the patient had tuberculous cavernes in both lungs, and progressive tuberculous changes in the ovaries and the ovi ducts, tuberculosis may have played a great part in causing the fatty liver, although the influence of the disturbance of the digestion and absorption due to the lack of pancreatic enzymes may not be neglected.

Case No. 4 : The patient died on the 344th postoperative day by chronic diarrhea and uremia caused by liver cirrhosis. The total liver lipides were 5.37 g/100g at autopsy. Hyperplasia of GLYSON'S capsel and round cell infiltration around it were revealed by microscopic examination. Parenchymal cells were

generally atrophic and bile pigments were found in some place. In short, we recognized biliary liver cirrhosis in this case, but intracellular fat granules were only a few, a finding contradictory to the fatty liver (Fig.F).

(6) Totally Depancreatized Dogs Treated with Neither Insulin Nor Other Drugs.:

This group consisted of 3 dogs. They died on the 3rd, 4th and 6th postoperative day respectively, and a marked increase in the total liver lipides was observed in all cases (Table 6). A marked fatty change of the liver was also demonstrated by microscopic examinations. But the fatty liver of this sort was of diabetic origin, and must be strictly distinguished from that appearing several weeks after total pancreatectomy.

Table 6 Total Liver Lipides in Totally Depancreatized Dogs Treated with Neither Insulin Nor Other Drugs.

Dog No.	Total liver lipides		Survival time days
	Biopsy at operation g/100g	at autopsy g/100g	
27	4.47	15.33	6
48	3.45	11.23	4
53	3.71	11.26	3

(7) Totally Depancreatized Dogs which Survived Less Than 3 Weeks Postoperatively :

It was stated by DRAGSTEDT et al in 1939 that the diabetic fatty liver developed immediately after operation and disappeared within two or three weeks after operation, if the experimental dogs were treated adequately with insulin. In my experiments, three dogs died earlier than 10 days after operation, and the liver lipides increased in these dogs (Table 7), and fatty change of the liver was observed by microscopic examination.

Table 7 Total Liver Lipides in Totally Depancreatized Dogs Surviving Less Than Three Weeks.

Dog No.	Total liver lipides		Survival time days
	Biopsy at operation g/100g	at autopsy g/100g	
15	3.20	6.83	9
17	4.47	10.1	4
20	4.32	8.38	4
22	4.42	3.98	16
49	3.00	3.57	22

On the other hand, in two dogs which died two or three weeks after operation, the amount of the total liver lipides was within the normal range (Table 7), even if they were treated only with insulin.

It seems therefore the true fatty liver, the development of which is prevented by the administration of pancreatin and methionine, appears later than 4 weeks after operation. These results coincide with those reported by previous authors.

(III) RELATION BETWEEN THE ESTER RATIO OF THE SERUM CHOLESTEROL AND THE TOTAL LIVER LIPIDES

There was no increase in the liver lipides, if the ester ratio determined for the last time before autopsy had been within the physiologic range (Table 8). Of the animals in which the last time ester ratio had declined below the physiologic range, 3 showed the increased liver lipides, while the other 6 were normal in the amount of the liver lipides. Therefore, it may be assumed that 1) there is no likelihood of developing the fatty liver when the ester ratio is within the physiologic range, and 2) not only the development of the fatty liver but also some other pathologic

Table 8 The Ester Ratio of the Serum Cholesterol and the Total Liver Lipides in Cases, Where the Last Time Ester Ratio was Within the Physiologic Range.

Dog No.	The last time ester ratio per cent	Total liver lipides at autopsy g/100g
5	77.0	2.61
7	88.1	3.59
8	84.7	2.36
9	81.6	3.29
16	88.1	2.83
18	84.5	3.76
28	84.2	3.12
40	92.4	3.19
41	90.4	5.34
43	79.1	4.64
47	89.1	3.54
49	91.3	3.57
60	90.2	5.08

Table 9 The Ester Ratio of the Serum Cholesterol and the Total Liver Lipides in Cases, Where the Last Time Ester Ratio was Lowered to the Level Below the Physiologic Range.

Dog No.	The last time ester ratio %	Total liver lipides at autopsy mg/100gm
6	56.4	2.32
10	52.6	2.10
14	38.4	3.08
22	56.3	3.93
26	56.2	3.12
37	66.0	4.84
27	21.2	15.33
35	45.2	12.4
48	49.7	11.2

condition of the liver is possible, when the ester ratio is lower.

DISCUSSION

The fatty liver, which has been believed to occur after total pancreatectomy in dogs since FISHER'S report, was not observed in my experimental animals except one, whether they might be given pancreatin and methionine or not. One of the reasons of this discrepancy in the results may lie in the mode of feeding, because my animals were fed with boiled rice and barley together with dried fish relatively poor in fat, instead of raw lean beef or horse meat.

The fatty liver in totally depancreatized men has been experienced in one exceptional case where the formation of tuberculous carvernes was found in both lungs. It is a well known fact that the fatty liver is apt to develop in certain cases of tuberculosis.

In 1953 K. HAMANO in our laboratory reported that a totally depancreatized man showed the better absorption rate of nutrients than a similarly treated dog. Takig this into consideration together with the fact that the fatty liver took place only in one case of my experimental dogs, the cause of the fatty liver after total pancreatectomy appears to be the lowering of the absorption rate of nutrients, especially of protein. Hence, the fatty liver of this sort may belong to the category of the dietary fatty liver.

It is worthy of note that the fatty liver in dogs was prevented completely by the administration of pancreatin and methionine, and that no fatty liver developed in men after total pancreatectomy except in one unusual case. Therefore, I believe, not only resection of the head of the pancreas but also total pancreatectomy can be performed in human cases of malignant neoplasms of the pancreas without much fear of the postoperative development of the fatty liver.

SUMMARRY AND CONCLUSION

(1) According to my study, the fatty liver, which had been believed to be common after total pancreatectomy in dogs, could be completely prevented by the administration of pancreatin and methionine. Even in dogs untreated with pancreatin and methionine the fatty liver developed only exceptionally.

These results are much different from those of previous authors. The reason may be in the difference in the mode of feeding after operation.

In men the fatty liver is more unlikely to occur after total pancreatectomy than in dogs.

(2) The fatty liver took place in no case of subtotal pancreatectomy or pancreatic duct ligation both in dogs and men.

(3) There occurred no fatty liver in those cases, in which the ester ratio of the serum cholesterol was within the physiologic range during life. Not only the development of the fatty liver but also some other liver damage must be taken into consideration when the ester ratio goes down to the level below the physiologic range.

(4) The fatty liver following total pancreatectomy may belong to the category of the dietary fatty liver

(5) If the indications are properly established, total pancreatoduodenectomy may be performed on men without much postoperative danger.

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和文抄錄

膵全剔后の脂肪肝：実験的並びに臨床的研究

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実験的に犬を使用して膵臓全剔出を行つた場合，術後適当にインスリンを投与するに拘らず，6～8週で高度の脂肪肝を発生し，為めに動物は斃死するに至ると云う事実は，1924年 Fisher 等によつて発表されて以来，一般に認められて居る，此の脂肪肝は膵全剔に特有のものとされ，その発生原因及び発生防止等に関する意見は区々であり，現在定説を見ない．故にわれわれは膵臓に悪性腫瘍が発生した場合，その唯一の根治的治療である膵全剔術を安全且つ良心的に施行し得る様にする為め，此の脂肪肝について実験的及び臨床的研究を行つた．

実験には成熟犬を使用し，膵十二指腸全剔術及び対照として，膵亜全剔術（残存膵組織 2～3g），膵管結紮術（十二指腸切除術）を施行した．

生前血清コレステリン・エステル商の推移により，脂肪肝の発生を窺知し，死後剖検時に肝総脂肪量を定量し，併せて肝組織のズダン Ⅲ による脂肪染色を行い，その発生を確かめ次の結果を得た，

1) 膵全剔後パンクレアチン5g，メチオニン 2g を毎日投与した犬に於ては，全例に於て脂肪肝の発生を見ず，又これ等薬剤を投与せざる犬に於ても，一例の例外を除き他の全例に脂肪肝の発生は認められなかつた．従来の報告とわれわれの実験結果の此の顕著な相違は実験動物に対する飼料の相違によると推定される．

2) 膵全剔臨床例は4例を検し得たが，内1例は術後3年の現在，元気に生存して居る．他の3例の内，肺，卵巣等に進行性結核病変を有した1例に於て，中心性肝脂肪変性を認めたが，本例の肝脂肪変性の主原因は，此の結核性病変によるものと思われる．

他の2例に於ては脂肪肝発生を見なかつた．

3) 教室浜野による消化吸収実験の結果と，以上の事実とより，膵全剔後特有のものと信じられて居た脂肪肝は食餌性脂肪肝の範疇に入れ得るものと考えられる．

4) 膵亜全剔，膵管結紮等の手術を施行した犬に於ては，全例に於て脂肪肝の発生を見なかつた．

5) 血清コレステリン・エステル商が生理的範囲内にある時には，脂肪肝の発生は否定し得る．血清コレステリン・エステル商の低下は，脂肪肝の発生によつて惹起されるのみならず，他の肝機能障害をも充分考慮せねばならぬ．

6) 以上の結果により，膵臓悪性腫瘍症例に対し，その適応が認められた場合には，術後発生すると云われた脂肪肝に対して，何等危惧するところなく，出来得る限り早期に膵全剔術，或いは膵頭部切除術を施行すべきものと信ずる．

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